

Food and Drug Administration. The raw data and results from each potency test performed shall be included.

(3) The product shall not be issued by the manufacturer until written notification of official release of the lot is received from the Director, Center for Biologics Evaluation and Research.

[41 FR 18295, May 3, 1976, as amended at 42 FR 27582, May 31, 1977; 49 FR 23834, June 8, 1984; 51 FR 15610, Apr. 25, 1986; 55 FR 11013, Mar. 26, 1990]

Subpart E—Bacillus of Calmette and Guérin (BCG) Vaccine

SOURCE: 44 FR 14545, Mar. 13, 1979, unless otherwise noted.

§ 620.40 BCG Vaccine.

(a) *Proper name and definition.* The proper name of this product is BCG Vaccine. The product is defined as a freeze-dried preparation containing viable bacteria of the *Bacillus of Calmette and Guérin*, which is an attenuated strain of *Mycobacterium bovis*.

(b) *Criteria for an acceptable strain.* The source of the BCG strain used in the manufacture of any lot of the final product must be identified by complete historical records.

(1) *Seed lot system.* The BCG strain must be maintained in the form of a primary seed lot that is to be the basic material from which all secondary seed lots are prepared. Production of BCG Vaccine may be from either primary or secondary seed lots. Each seed lot must be stored in either a freeze-dried state at -20°C or colder, or in a frozen state at -70°C or colder.

(2) *Freedom from virulence.* The BCG strain is demonstrated to be incapable of producing progressive tuberculosis in guinea pigs tested as prescribed in § 620.45, except that no fewer than 48 guinea pigs must be used to test the primary seed lot and no fewer than 12 guinea pigs must be used to test each secondary seed lot. At least two-thirds of the animals must survive the observation period of no less than 6 months.

(3) *Induction of tuberculin sensitivity in guinea pigs.* Each of at least 10 guinea pigs is to be injected with 1 human dose of BCG Vaccine and, within 4 to 6 weeks after vaccination, skin tested with tuberculin. At least 80 percent of

the guinea pigs tested must develop tuberculin sensitivity, as prescribed in § 620.44(b)(3)(ii).

(4) *Clinical information.* Clinical data must establish that the BCG strain is safe and induces tuberculin sensitivity. After having passed all laboratory tests prescribed for BCG Vaccine, each primary and secondary seed lot of vaccine must be tested for its ability to induce sensitivity in tuberculin-negative persons. Only those persons tested by injection of 5 U.S. Tuberculin Units, Purified Protein Derivative, by the Mantoux technique and found negative in this test are to be selected for clinical trials. At least 100 tuberculin-negative persons must be included in the test of the primary seed lot, and at least 20 tuberculin-negative persons must be included in the test of each secondary seed lot. Within 6 to 8 weeks after BCG vaccination, the vaccinees must be tested for tuberculin reactivity by injecting not more than 10 U.S. Tuberculin Units, Purified Protein Derivative, by the Mantoux technique. The test is considered satisfactory if a least 90 percent of those persons from each group develop tuberculin reactivity as indicated by an induration reaction of at least 5 millimeters in diameter.

§ 620.41 Establishment and personnel requirements.

In addition to the applicable requirements of §§ 600.10 and 600.11 of this chapter, the following practices and procedures are required:

(a) *Isolation of BCG unit.* (1) A BCG unit is defined as the space used for storage of primary and secondary seed cultures and for vaccine preparation, including culture maintenance, media inoculation for propagation, harvesting, filling into final containers, sealing of final containers, media production, and cleaning and sterilization of glassware. For purposes of these additional standards, the space used for incubation of bulk and final container sterility tests, tests to determine the numbers of colony-forming units, animal tests, and necropsies are not part of the BCG unit.

(2) The BCG unit must be completely isolated from other production and surrounding areas and must be situated